Please cancel Claims 29-31, without prejudice to, or disclaimer of, the subject matter contained therein.

Please add the following new Claim 35:

35. (NEW) An isolated polypeptide comprising the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 203538.

REMARKS

Applicants amended Claim 27 and have cancelled Claims 22-26 and 29-31, without prejudice to, or disclaimer of, the subject matter contained therein, and have added new Claim 35. The new Claim 35 is directed to the subject matter of subsection (e) of the old Claim 27. The reasons for the amendments are set forth in detail below. The specific changes to the amended claims are shown on a separate set of pages attached hereto and entitled VERSION WITH MARKINGS TO SHOW CHANGES MADE, which follows the signature page of this Amendment. On this set of pages, the insertions are underlined, while the deletions are **[bracketed and in bold]**.

Applicants respond below to the specific rejections and objections raised by the Examiner in the Office Action of June 14, 2002.

I. Objections and Rejections under 35 U.S.C. § 101

Claims 22-34 stand rejected under 35 U.S.C. § 101 for allegedly lacking specific, substantial, and credible asserted utility or a well established utility. For the reasons set forth below, Applicants respectfully traverse.

Utility – Legal Standard

According to the Utility Examination Guidelines ("Utility Guidelines"), 66 Fed. Reg. 1092 (2001) an invention complies with the utility requirement of 35 U.S.C. § 101, if it has at least one asserted "specific, substantial, and credible utility" or a "well-established utility."

[redacted]

Under the Utility Guidelines, a utility is "specific" when it is particular to the subject matter claimed. For example, it is generally not enough to state that a nucleic acid is useful as a diagnostic without also identifying the condition that is to be diagnosed.

The requirement of "substantial utility" defines a "real world" use, and derives from the Supreme Court's holding in *Brenner v. Manson*, 383 U.S. 519, 534 (1966) stating that "The basic *quid pro quo* contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility." In explaining the "substantial utility" standard, M.P.E.P. 2107.01 cautions, however, that Office personnel must be careful not to interpret the phrase "immediate benefit to the public" or similar formulations used in certain court decisions to mean that products or services based on the claimed invention must be "currently available" to the public in order to satisfy the utility requirement. "Rather, *any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient,* at least with regard to defining a "substantial" utility." (M.P.E.P. 2107.01, emphasis added.) Indeed, the Guidelines for Examination of Applications for Compliance With the Utility Requirement, set forth in M.P.E.P, 2107 II (B) (1) gives the following instruction to patent examiners: "If the applicant has asserted that the claimed invention is useful for any particular practical purpose . . . and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility."

Finally, the Utility Guidelines restate the Patent Office's long established position that any asserted utility has to be "credible." "Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record . . . that is probative of the applicant's assertions." (M.P.E.P. 2107 II (B) (1) (ii)) Such standard is presumptively satisfied unless the logic underlying the assertion is seriously flawed, or if the facts upon which the assertion is based are inconsistent with the logic underlying the assertion (Revised Interim Utility Guidelines Training Materials, 1999).

Proper Application of the Legal Standard

Applicants submit that the gene amplification data provided in the present application are sufficient to establish a specific, substantial and credible utility for the PRO1800 polypeptide.

[redacted]

Gene amplification is an essential mechanism for oncogene activation. It is well known that gene amplification occurs in most solid tumors, and generally is associated with poor prognosis. As described in Example 16 of the present application, the inventors isolated genomic DNA from a variety of primary cancers and cancer cell lines that are listed in Table 7 (page 117 of the specification). As a negative control, DNA was isolated from the blood of normal healthy individuals (page 115, lines 22-33). Gene amplification was monitored using real-time quantitative TaqMan™ PCR. The gene amplification results are set forth in Table 7. As explained on page 112, lines 17-19, the results of TaqMan™ PCR are reported in ΔCt units. One unit corresponds to one PCR cycle or approximately a 2-fold amplification, relative to control, two units correspond to 4-fold, 3 units to 8-fold, etc. amplification.

Applicants respectfully note that the Examiner's recounting of the gene amplification results is contrary to the teachings of the specification. First, the Examiner states that "At page 113, ΔCt is defined as the threshold PCR cycle." Actually, the specification at page 113 defines Ct, and not ΔCt, as the threshold PCR cycle. In fact, it is well-known in the art that "Ct" stands for "threshold cycle."

Second, the Examiner states that neither the specification nor the art provide "an explanation of how ΔCt values are calculated, nor what the significance of such are." Applicants respectfully disagree. It is well-known in the art how ΔCt values are calculated. The TaqMan™ real-time PCR method, which is the used in the methods of the present application, has gained wide recognition for its versatility, sensitivity and accuracy, and is in extensive use for the study of gene amplification. The TaqMan™ 7700 Sequence Detector Software calculates the Ct values for each given experiment. Those of skill in the art know that to obtain ΔCt, the difference between the Ct values of the test sample and the normal sample is calculated. Furthermore, the specification itself teaches that "The diluted samples were used provided that the Ct value of the normal human DNA subtracted from test DNA was +/- 1 Ct." Specification at page 116, lines 30-31. Thus, the specification teaches that ΔCt is obtained when the Ct value of the normal sample is subtracted from the Ct value of the test sample.

As for the significance of the data, the specification states that one ΔCt unit corresponds to two-fold amplification, two units to four-fold, three units to 8-fold, etc. This fact is also well-

known in the art. Thus, the significance of knowing the ΔCt value is that the extent of gene amplification in a cancer cell is known.

As set forth on page 85, lines 34-37, the disclosed proteins of the invention can be used for tissue typing. Table 7 identifies several tissue types, all obtained from cancerous tumors, in which PRO1800 is amplified. PRO1800 can then be used diagnostically in determining whether a particular tissue type obtained from a patient is cancerous or not. Thus, those of skill in the art recognize the utility of the PRO1800 polypeptide as a diagnostic tool. This utility is specific, since it applies only to those polypeptides where the overexpression of their genes is established, i.e., PRO1800. The utility is also credible, because those of skill in the art recognize that having a diagnostic tool to identify cancer tissues before they have advanced to the point where the disease compromises the life-span of the individual patient is quite attractive. Furthermore, the utility is substantial since it can potentially alert medical professionals to the presence of cancer at an early stage when treatment is facile and feasible.

Based on the 35 U.S.C. § 101 arguments, the Examiner has also rejected the claims on the grounds of 35 U.S.C. § 112. Since the Applicants respectfully submit, based on the above arguments, that the claims enjoy an assertion of utility that satisfies the requirements of § 101, Applicants respectfully submit that the § 112 rejections are now moot.

In view of the above, Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

II. Rejections under 35 U.S.C. § 112, First Paragraph

Claims 22-34 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly containing a subject matter which is not described in the specification in such a way as to convey to one of skill in the art that the inventor had possession of the application. Applicants respectfully submit that in view of the amendments submitted herein, the rejections are now moot and respectfully request that the Examiner withdraw the rejections.

III. Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 22-34 stand rejected under 35 U.S.C. § 112, second paragraph. Applicants respectfully submit that in view of the amendments submitted herein, the rejections are now moot and respectfully request that the Examiner withdraw the rejections.

IV. Rejections under 35 U.S.C. §§ 102 and 103

Claims 22-34 stand rejected under 35 U.S.C. §§ 102 and 103. Applicants respectfully submit that since a proper assertion of utility has been made, Applicants are entitled to their claim of priority, which is February 11, 2000, the filing date of the International Application Serial No. PCT/US00/03565, from which the present application claims priority. Thus, the Strausberg and Furukawa references, having a publication date after the priority date of the present application, are removed as prior art, and all rejections based on these two references are now moot.

Furthermore, Applicants have cancelled the claims 22-26, which are directed to the polypeptide molecules having less than 100% identity to SEQ ID NO:2. Since neither Fransen reference discloses the full-length amino acid sequence of SEQ ID NO:2, the pending claims are novel and non-obvious over these cited references.

Applicants, therefore, request that the Examiner reconsider and withdraw the rejections based on 35 U.S.C. §§ 102 and 103.

CONCLUSION

Applicants respectfully maintain that claims are patentable and request that they be passed to issue. A check in the amount of $920.00 is enclosed in connection with a petition for a three month extension of time, which allows for a timely response to be filed on or before December 14, 2002. If the enclosed fee is incorrect, the Commissioner is hereby authorized to charge or credit Deposit Account No. 11-1410. Applicants invite the Examiner to call the undersigned if any issues may be resolved through a telephonic conversation.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: December 11, 2002

By: _____

Sam K. Tahmassebi
Registration No. 45,151
Attorney of Record
2040 Main Street
Fourteenth Floor
Irvine , CA 92614
(619) 235-8550

AMEND

S:\DOCS\SKT\SKT-3011.DOC
121002

VERSION WITH MARKINGS TO SHOW CHANGES MADE.

Please cancel Claims 22-26, without prejudice to, or disclaimer of, the subject matter contained therein.

27. (ONCE AMENDED) An isolated polypeptide comprising**[:**

(a)] the amino acid sequence of the polypeptide shown in Figure 2 (SEQ ID NO:2)**[;**

(b) the amino acid sequence of the polypeptide shown in Figure 2 (SEQ ID NO:2), lacking its associated signal peptide;

(c) the amino acid sequence of the extracellular domain of the polypeptide shown in Figure 2 (SEQ ID NO:2);

(d) the amino acid sequence of the extracellular domain of the polypeptide shown in Figure 2 (SEQ ID NO:2), lacking its associated signal peptide; or

(e) the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 203538].

Please cancel Claims 29-31, without prejudice to, or disclaimer of, the subject matter contained therein.

Please add the following new Claim 35:

35. (NEW) An isolated polypeptide comprising the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 203538.